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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,400	08/26/2003	William E. Bunney JR.	020885-000720US	6108

20350 7590 07/26/2006

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
STANDLEY, STEVEN H	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 07/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/649,400	BUNNEY ET AL.	
	Examiner	Art Unit	
	Steven H. Standley	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,8-11 and 51* is/are pending in the application.

4a) Of the above claim(s) *10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 8-9, 11 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendment filed 5/17/06 has been made of record. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Objections/Rejections: Withdrawn

Claim Rejections - 35 USC § 112

Rejection of claims 1, 3, 8-9, 11 under 35 USC § 112, 1st total lack of enablement is withdrawn due to applicant's amendment.

Rejection of claims 1, 3, 8-9, 11 under 35 USC § 112, 2d for omitting essential steps is withdrawn due to applicant's amendment.

Rejection of claims 1, 3, 8-9, 11 under 35 USC § 112, 2d reciting indefinite 'stringent conditions 'is withdrawn due to applicant's amendment.

Objections/Rejections: Maintained/New Grounds

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 8-9, 11 and newly submitted claim 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of diagnosing a subject with a mental disorder comprising the steps of obtaining a biopsy sample from a live or dead patient consisting of layers 3-6 of the dorsal lateral prefrontal cortex, contacting said sample tissue with a nucleic acid fully complementary to that of SEQ ID NO 3 and comparing the detected level of the nucleic acid to that of an age and neuroanatomically-matched control, does not reasonably provide enablement for isolating a subject's brain tissue and contacting with a reagent and comparing the detected level of reagent with a control. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of Applicant's recited invention now reads "A method for determining whether a subject ***has*** or is ***predisposed*** for a mental disorder, the method comprising the steps of: ***isolating a subjects brain tissue...[emphasis added].***" However, this

is complex because it recites, "isolating the subjects brain tissue" when reasonably the only brain region that exhibits any diagnostic value is the dorsolateral prefrontal cortex. Secondly, there is no disclosure in the specification or the art as to whether the increase in expression level ***precedes*** the onset of the mental illness, and is ***predictive*** of a predisposition for a mental disorder. Thus, the nature of the invention is complex because it relies on tissues with unknown and undisclosed diagnostic value, and asserts predictive value when only ***post hoc*** diagnostic value is apparent.

The prior art is silent as to whether additional regions of the brain would be useful to diagnose bipolar illness or any other mental illness by detecting TBR1 mRNA. However, the instant disclosure indicates the difference is only 30% and only in layers 3-6, and not 1-2 of the dorsolateral prefrontal cortex. This indicates, because at least layer II contains pyramidal cell and stellate cell bodies--therefore should contain abundant mRNA--that overexpression even in an adjacent region of the cortex is entirely unpredictable.

There are no working examples of instructing as to the value of TBR1 mRNA in determining whether a patient is predisposed to mental illness, or for value in obtaining or using any other brain region for predicting or diagnosing mental illness. Further, there is no guidance as to how one of skill in the art would use other areas of the brain or use TBR1 mRNA to determine whether a patient is predisposed to a mental disorder.

The breadth of the claims is such that they encompass brain regions with unknown, undisclosed, and unpredictable value for diagnosing a mental disorder. The

breadth of the claims is such that they encompass prediction of subsequent mental disorder, which is neither supported by the specification or the art.

Thus, considering the nature of the invention, the state of the art, the unpredictability of the art, the lack of examples or guidance in the specification, and the breadth of the claims one skilled in the art would not be able to use the invention without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 8-9, 11 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Typically, a polynucleotide is not 'encoded' by a nucleic acid per se. Simply omitting 'encoded by a nucleic acid' would obviate the rejection. Claims 3, 8-9, 11, and 51 are rejected because they depend from an indefinite claim.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven H. Standley whose telephone number is (571) 272-3432. The examiner can normally be reached on 8:00-4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Janet Andre can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Steven Standley, Ph.D.

7/21/05

David Romeo

DAVID S. ROMEO
PRIMARY EXAMINER